

## CLAIMS

1. A method for detecting a risk of hypertension in a subject by determining the pattern of alleles encoding a variant  $\alpha_{2B}$ -adrenoceptor, comprising the steps of
  - 5 a) providing a biological sample of the subject to be tested,
  - b) providing an assay for detecting in the biological sample the presence of
    - i) the insertion/insertion (I/I) or deletion/insertion (D/I) genotypes of the human  $\alpha_{2B}$ -adrenoceptor, or
    - ii) the D/D genotype of the human  $\alpha_{2B}$ -adrenoceptor, the presence of the D/D genotype indicating an increased risk of hypertension in said subject.
- 10 2. The method according to claim 1, wherein the assay is a DNA-assay.
3. The method according to claim 1 or 2, wherein the assay is carried out using a gene or DNA chip, microarray, strip, panel or similar combination of more than one genes, mutations or RNA expressions to be assayed.
- 15 4. The method according to claim 1, wherein the allelic pattern is determined using polymerase chain reaction.
5. The method according to claim 1, wherein the biological sample is a blood sample or buccal sweep sample and genomic DNA is isolated from the said sample.
- 20 6. The method according to claim 1, wherein the assay is based on a capturing probe which comprises a single strand of the cDNA, comprising a nucleotide sequence encoding a variant  $\alpha_{2B}$ -adrenoceptor protein with a deletion of at least 1 glutamate from a glutamic acid repeat element of 12 glutamates, amino acids 298–309, in an acidic stretch of 18 amino acids 294–311, located in
  - 25 the 3<sup>rd</sup> intracellular loop of the receptor polypeptide.

7. The method according to claim 1, wherein the assay is based on a capturing probe which comprises a single strand of the cDNA corresponding to the  $\alpha_{2B}$ -adrenoceptor without the deletion of a glutamate from a glutamic acid repeat element of 12 glutamates, amino acids 298–309, in an acidic stretch of 18 amino acids 294–311, located in the 3<sup>rd</sup> intracellular loop of the receptor polypeptide.
8. The method according to claim 1, wherein the said method is used for determining whether a subject will benefit from treatment with a drug affecting the noradrenaline sensitivity or sympathetic activity of the subject.
9. The method according to claim 1, wherein the said method is used for determining whether a subject will benefit from treatment with an  $\alpha_{2B}$ -adrenoceptor antagonist.
10. The method according to claim 1, wherein the said method is used for determining whether a subject will be at increased risk of adverse effects if subtype-nonspecific  $\alpha_2$ -agonists or a diuretic or a calcium channel blocker are administered to them.
11. The method according to claim 1, comprising the step of selecting a subject of the D/D genotype for clinical drug trials testing the antihypertensive effects of compounds.
12. The method according to claim 11, wherein the said compound is a drug affecting the noradrenaline sensitivity or sympathetic activity of the subject.
13. The method according to claim 8 or 11, wherein the said compound is a drug modulating, inhibiting or activating the vascular alpha- or beta-adrenergic receptors of the subjects either directly or through central nervous system effects.

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14. The method according to claim 8 or 11, wherein the said compound is an angiotensin converting enzyme (ACE) inhibitor, angiotensin II inhibitor or angiotensin receptor inhibitor.

15. The method according to claim 13, wherein the said compound is an  $\alpha_{2B}$ -selective or  $\alpha_{2B}$ -nonselective  $\alpha_2$ -adrenoceptor antagonist.

16. A method for targeting the treatment of hypertension in a hypertensive subject by determining the pattern of alleles encoding a said variant  $\alpha_{2B}$ -adrenoceptor, i.e. by determining if said subject's genotype of the human  $\alpha_{2B}$ -adrenoceptor is of the deletion/deletion (D/D) type, comprising the steps presented in claim 1, and treating a subject of the D/D genotype with a drug affecting the noradrenaline sensitivity or sympathetic activity of the subject.

17. The method according to claim 16, wherein the said drug is a drug modulating, inhibiting or activating the vascular alpha- or beta-adrenergic receptors of the subjects either directly or through central nervous system effects.

18. The method according to claim 17, wherein the said drug is pindolol, propranolol, sotalol, timolol, acebutolol, atenol, betaxolol, bisoprol, esmolol, metoprolol, seliprol, carvedilol, labetalol, clonidine, moxonidine, prazosin, or indapamid.

19. The method according to claim 16, wherein the said drug is an angiotensin converting enzyme (ACE) inhibitor, angiotensin II inhibitors or angiotensin receptor inhibitor.

20. The method according to claim 19, wherein the said drug is captopril, cinapril, enalapril, imidapril, lisinopril, moexipril, perindopril, ramipril, trandolapril, candesartan, eprosartan, irbesartan, losartan, valsartan or telmisartan.

21. A method according to claim 17, wherein the said drug is an  $\alpha_{2B}$ -selective or  $\alpha_{2B}$ -nonselective  $\alpha_2$ -adrenoceptor or  $\alpha$ -adrenoceptor antagonist.

22. A kit for detecting a risk of hypertension in a subject, or for selecting a subject for targeting antihypertensive treatment, or for selecting a subject for clinical drug trials testing the antihypertensive effect of compounds, comprising means for determining the pattern of alleles encoding a variant  $\alpha_{2B}$ -adrenoceptor in a biological sample from said subject, and optionally software to interpret the results of the determination.

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23. The use of the kit according to claim 22 for detecting a risk of hypertension in a subject, or for selecting a subject for targeting antihypertensive treatment, or for selecting a subject for clinical drug trials testing the antihypertensive effect of compounds.

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